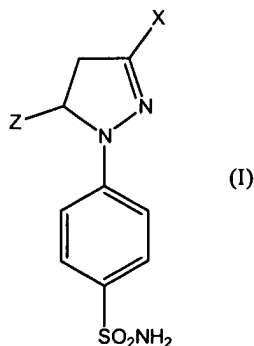


Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Amended) A compound of the formula I:



wherein:

X is [selected from the group consisting of] trihalomethyl [and C₁-C₆ alkyl]; and
Z is selected from the group consisting of substituted and unsubstituted aryl other than substituted and unsubstituted phenyl; or a pharmaceutically acceptable salt thereof.

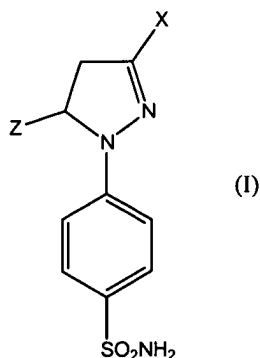
2. (Original) A compound according to claim 1 wherein Z is selected from the group consisting of substituted and unsubstituted heteroaryl; or a pharmaceutically acceptable salt thereof.

3. (Twice amended) A compound according to claim 2 wherein [[Z]] said heteroaryl is selected from the group consisting of [substituted and unsubstituted] indolyl, furyl, thienyl, pyridyl, benzofuryl, benzothienyl, imidazolyl, pyrazolyl, thiazolyl, [benzothazolyl] benzothiazolyl, quinolinyl, and 4-(2-benzyloxazolyl); or a pharmaceutically acceptable salt thereof.

4. (Original) A compound according to claim 1 wherein Z is 3-indolyl; or a pharmaceutically acceptable salt thereof.

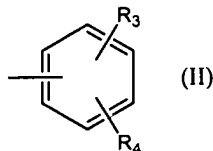
5. (Original) A compound according to claim 1 wherein X is trifluoromethyl.

6. (Twice amended) A compound of the formula I:



wherein:

X is a group of formula II:



wherein:

R₃ and R₄ are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; carboxy; C₁-C₆ trihaloalkyl; and cyano;

Z is selected from the group consisting of substituted and unsubstituted heteroaryl; phenyl which is mono-substituted with hydroxyl, nitro, carboxy, C₁-C₆ trihaloalkyl or cyano; phenyl which is di-substituted; and phenyl which is tri-substituted; [aryl, and]

provided when Z is substituted or unsubstituted heteroaryl, it is selected from the group consisting of [substituted and unsubstituted] pyridyl, furyl, indolyl, benzothienyl, benzofuryl, imidazolyl, pyrazolyl, 2-thiazolyl, quinolinyl and 4-(2-benzyloxazolyl);

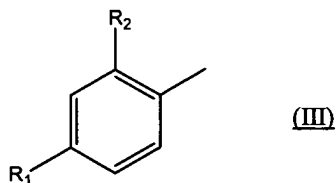
or a pharmaceutically acceptable salt thereof.

7. (Twice amended) A compound according to claim 6 wherein Z is selected from the group consisting of [unsubstituted phenyl; and] phenyl mono-substituted with

hydroxyl, nitro, carboxy, C₁-C₆ trihaloalkyl or cyano, [[di-]] di-substituted phenyl and tri-substituted phenyl.

8. (Amended) A compound according to claim 7 wherein Z is phenyl substituted with one or more of [halogen,] hydroxyl, nitro, [C₁-C₆ alkyl, C₁-C₆ alkoxy,] or carboxy; or a pharmaceutically acceptable salt thereof.

9. (Amended) A compound according to claim [10] 6 wherein Z is the group:



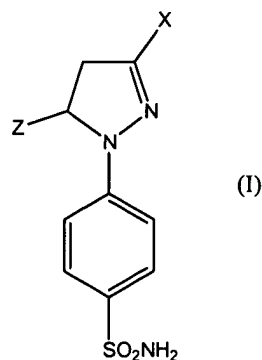
wherein R₁ and R₂ are independently selected from the group consisting of [hydrogen,] fluorine, bromine, chlorine, C₁-C₃ alkyl, C₁-C₃ alkoxy, hydroxyl and nitro; or a pharmaceutically acceptable salt thereof.

10. (Amended) A compound according to claim 6 wherein Z is substituted or unsubstituted heteroaryl, wherein said heteroaryl is indolyl, furyl, pyridyl or benzofuryl; or a pharmaceutically acceptable salt thereof.

11. (Original) A compound according to claim 10 wherein Z is substituted or unsubstituted 3-indolyl; or a pharmaceutically acceptable salt thereof.

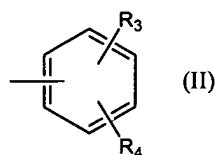
12. (Original) The compound according to claim 1 which is 1-(4-sulfamylphenyl)-3-trifluoromethyl-5-(3-indolyl)-2-pyrazoline; or a pharmaceutically acceptable salt thereof.

13. (Amended) A compound of the formula I:



wherein:

X is a group of formula II:

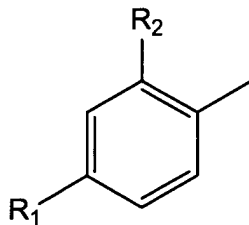


wherein:

R₃ and R₄ are independently selected from the group consisting of hydrogen, C₁-C₆ alkyl and C₁-C₆ alkoxy;

Z is selected from the group consisting of [phenyl;] phenyl monosubstituted with [halogen,] hydroxyl, nitro or carboxy; disubstituted phenyl; trisubstituted phenyl; and substituted and unsubstituted heteroaryl, wherein said heteroaryl is selected from the group consisting of [substituted and unsubstituted] pyridyl, furyl, indolyl, benzothienyl, benzofuryl, imidazolyl, pyrazolyl, 2-thiazolyl, quinolinyl and 4-(2-benzylloxazolyl); or a pharmaceutically acceptable salt thereof.

14. (Amended) A compound according to claim 13 wherein Z is the group:

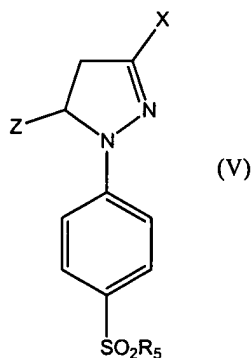


wherein R₁ and R₂ are independently selected from the group consisting of fluorine, bromine, chlorine, C₁-C₃ alkyl, C₁-C₃ alkoxy, hydroxyl and nitro; or a pharmaceutically acceptable salt thereof.

15. (Amended) A compound according to claim 13 wherein Z is substituted or unsubstituted heteroaryl, wherein said heteroaryl is indolyl, furyl, pyridyl or benzofuryl; or a pharmaceutically acceptable salt thereof.

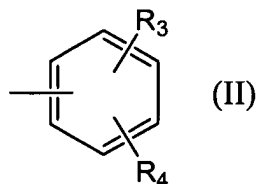
16. (Original) A compound according to claim 15 wherein Z is substituted or unsubstituted 3-indolyl; or a pharmaceutically acceptable salt thereof.

17. (Amended) A compound of the formula V:



wherein:

X is selected from the group consisting of trihalomethyl, C₁-C₆ alkyl, and a group of formula II:

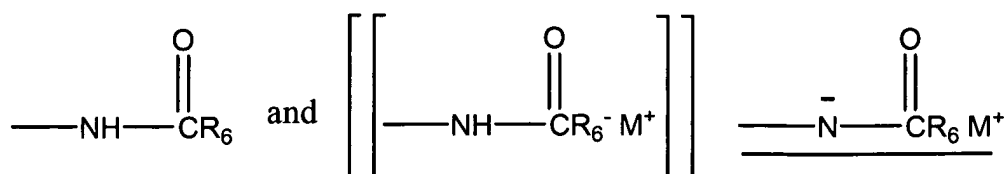


wherein:

R₃ and R₄ are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C₁-C₆ alkyl; C₁-C₆ alkoxy; carboxy; C₁-C₆ trihaloalkyl; and cyano;

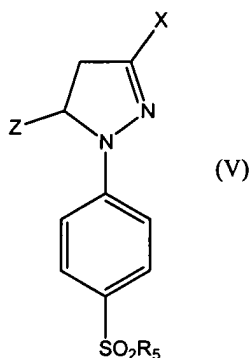
Z is substituted or unsubstituted heteroaryl; and

R₅ is selected from the group consisting of:



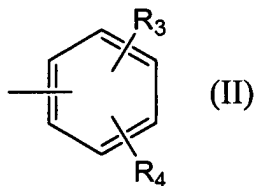
wherein R₆ is C₁-C₆ alkyl and M is Na, K or Li; or a pharmaceutically acceptable salt thereof.

18. (Amended) A compound of the formula V:



wherein:

X is a group of formula II:

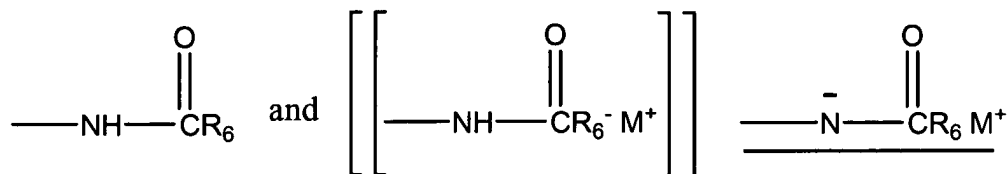


wherein:

R₃ and R₄ are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C₁-C₆ alkyl; C₁-C₆ alkoxy; carboxy; C₁-C₆ trihaloalkyl; and cyano;

Z is selected from the group consisting of substituted and unsubstituted aryl; and

R₅ is selected from the group consisting of:



wherein R₆ is C₁-C₆ alkyl and M is Na, K or Li or a pharmaceutically acceptable salt thereof.

19. (Original) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to claim 17 or 18, or a pharmaceutically acceptable salt thereof.

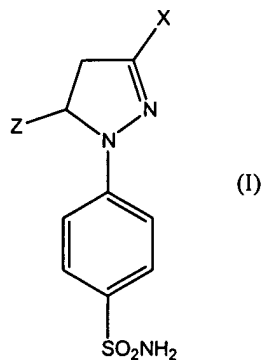
20. (Amended) A method for treating a cyclooxygenase-2-mediated disorder comprising administering to a patient in need of such treatment an effective amount of a compound according to claim 17 or 18, or a pharmaceutically acceptable salt thereof.

21. (Amended) A method for treating inflammation or an inflammation-mediated disorder, wherein said inflammation or inflammation-mediated disorder is mediated by cyclooxygenase-2, comprising administering to a subject in need of such treatment an effective amount of a compound according to claim 17 or 18, or a pharmaceutically acceptable salt thereof.

22. (Amended) A method for treating a neoplasia, wherein said neoplasia is mediated by a cyclooxygenase-2, comprising administering to a subject in need of such treatment an effective amount of a compound according to claim 17 or 18, or a pharmaceutically acceptable salt thereof.

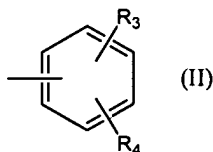
23. (Amended) A method for treating an angiogenesis-mediated disorder, wherein said angiogenesis-mediated disorder is mediated by a cyclooxygenase-2, administering to a subject in need of such treatment an effective amount of a compound according to claim 17 or 18, or a pharmaceutically acceptable salt thereof.

24. (Twice amended) A method for producing a compound of formula I:



wherein:

the group X is [selected from the group consisting of] trihalomethyl[, C₁-C₆ alkyl, and a radical of formula II:



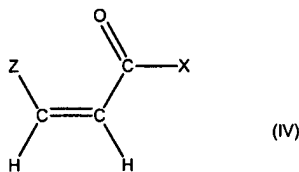
wherein:

wherein R₃ and R₄ are independently selected from the group consisting of hydrogen, halogen, hydroxyl, nitro, C₁-C₆ alkyl, C₁-C₆ alkoxy; carboxy; C₁-C₆ trihaloalkyl; and cyano]; and

Z is selected from the group consisting of substituted and unsubstituted aryl, other than substituted and unsubstituted phenyl;

the method comprising:

(a) reacting a compound of the formula IV:



wherein X and Z are so defined;

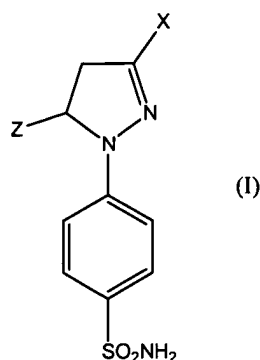
with 4-sulfamyl phenyl hydrazine or a salt thereof; and

(b) isolating a compound according to formula I from the reaction products.

25. (Original) A method according to claim 24 wherein Z is substituted or unsubstituted heteroaryl.

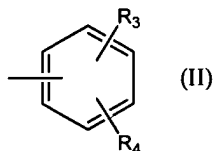
26. (Canceled)

27. (Twice amended) A method for producing a compound of formula I:



wherein:

the group X is a radical of formula II:



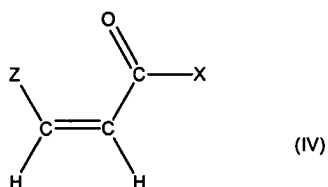
wherein:

[wherein] R₃ and R₄ are independently selected from the group consisting of hydrogen, halogen, hydroxyl, nitro, C₁-C₆ alkyl, C₁-C₆ alkoxy; carboxy; C₁-C₆ trihaloalkyl; and cyano; and

Z is selected from the group consisting of substituted and unsubstituted [aryl] heteroaryl; phenyl which is mono-substituted with hydroxyl, nitro, carboxy; C₁-C₆ trihaloalkyl or cyano; phenyl which is di-substituted, and phenyl which is tri-substituted;

the method comprising:

(a) reacting a compound of the formula IV:

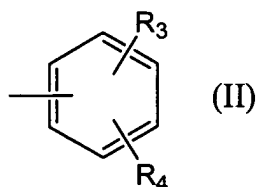


wherein X and Z are so defined;

with 4-sulfamyl phenyl hydrazine or salt thereof; and

(b) isolating a compound according to formula I from the reaction products.

28. (Amended) A method according to claim 27 wherein the group X in the reactant compound of formula IV is a radical of formula II:

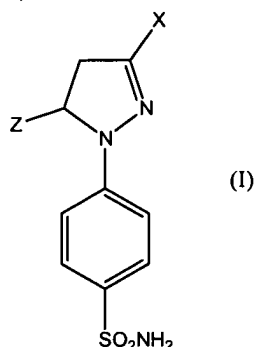


wherein:

[wherein] R₃ and R₄ are independently selected from the group consisting of hydrogen, halogen, hydroxyl, nitro, C₁-C₆ alkyl, C₁-C₆ alkoxy; and carboxy.

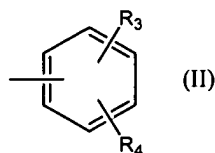
29. (Original) An isolated optical isomer of a compound according to claim 17 or 18, or a pharmaceutically acceptable salt thereof.

30. (Amended) An isolated optical isomer of a compound of the formula I:



wherein:

X is [selected from the group consisting of trihalomethyl, C₁-C₆ alkyl, and] a group of formula II:



wherein:

R₃ and R₄ are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C₁-C₆ alkyl; C₁-C₆ alkoxy; carboxy; C₁-C₆ trihaloalkyl; and cyano;

Z is selected from the group consisting of substituted and unsubstituted aryl;

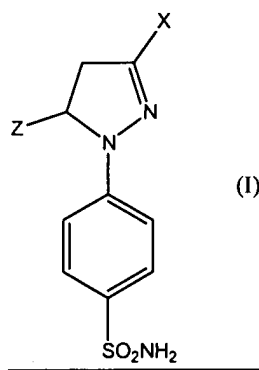
or a pharmaceutically acceptable salt thereof.

31. (Original) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to claim 1.

32. (Original) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to claim 6.

33. (Original) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to claim 13.

34. (Twice amended) A method for treating a cyclooxygenase-2-mediated disorder comprising administering to a patient in need of such treatment an effective amount of a compound according to [claim 1] formula I:

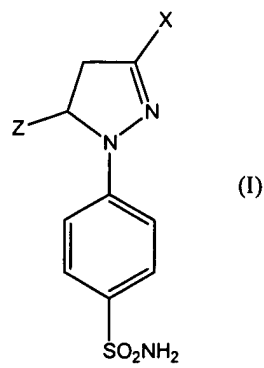


wherein:

X is selected from the group consisting of trihalomethyl and C₁-C₆ alkyl;

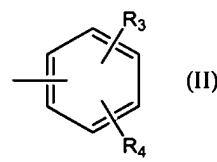
Z is selected from the group consisting of substituted and unsubstituted aryl other than substituted and unsubstituted phenyl; or a pharmaceutically acceptable salt thereof.

35. (Thrice amended) A method for treating a cyclooxygenase-2-mediated disorder comprising administering to a subject in need of such treatment an effective amount of a compound according to [claim 6] formula I:



wherein:

X is a group of formula II:



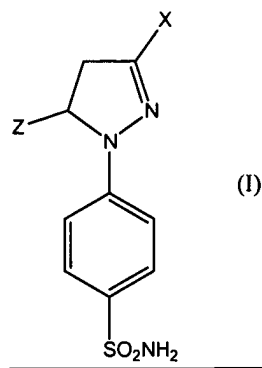
wherein:

R₃ and R₄ are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; carboxy; C₁-C₆ trihaloalkyl; and cyano;

Z is selected from the group consisting of substituted and unsubstituted aryl, and substituted and unsubstituted heteroaryl;

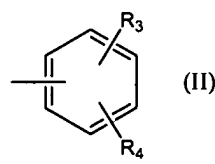
wherein said heteroaryl is selected from the group consisting of pyridyl, furyl, indolyl, benzothienyl, benzofuryl, imidazolyl, pyrazolyl, 2-thiazolyl, quinolinyl and 4-(2-benzyloxazolyl); or a pharmaceutically acceptable salt thereof.

36. (Thrice Amended) A method for treating a cyclooxygenase₂-mediated disorder comprising administering to a subject in need of such treatment an effective amount of a compound according to [claim 13] formula I:



wherein:

X is a group of formula II:

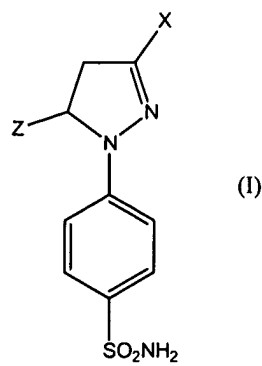


wherein:

R₃ and R₄ are independently selected from the group consisting of C₁-C₆ alkyl and C₁-C₆ alkoxy;

Z is selected from the group consisting of phenyl; phenyl monosubstituted with halogen, hydroxyl, nitro or carboxy; disubstituted phenyl; trisubstituted phenyl; and substituted and unsubstituted heteroaryl, wherein said heteroaryl is selected from the group consisting of pyridyl, furyl, indolyl, benzothienyl, benzofuryl, imidazolyl, pyrazolyl, 2-thiazolyl, quinoliny and 4-(2-benzyloxazolyl); or a pharmaceutically acceptable salt thereof.

37. (Twice amended) A method for treating inflammation or an inflammation-mediated disorder, wherein said inflammation or inflammation-mediated disorder is mediated by a cyclooxygenase-2, comprising administering to a subject in need of such treatment an effective amount of a compound according to [claim 1] formula I:

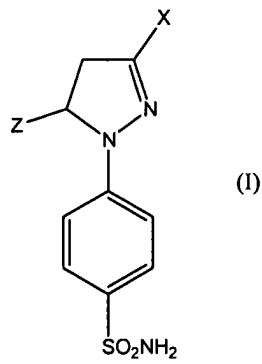


wherein:

X is selected from the group consisting of trihalomethyl and C₁-C₆ alkyl;

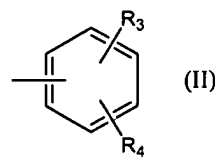
Z is selected from the group consisting of substituted and unsubstituted aryl other than substituted and unsubstituted phenyl; or a pharmaceutically acceptable salt thereof.

38. (Twice amended) A method for treating inflammation or an inflammation-mediated disorder, wherein said inflammation or inflammation-mediated disorder is mediated by a cyclooxygenase-2, comprising administering to a subject in need of such treatment an effective amount of a compound according to [claim 6] formula I:



wherein:

X is a group of formula II:

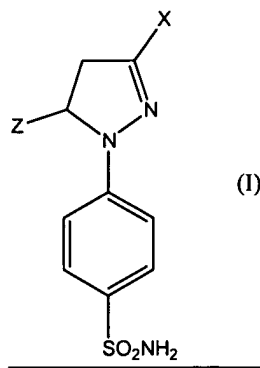


wherein:

R₃ and R₄ are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; carboxy; C₁-C₆ trihaloalkyl; and cyano;

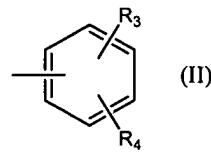
Z is selected from the group consisting of substituted and unsubstituted aryl, and when Z is heteroaryl, it is selected from the group consisting of substituted and unsubstituted pyridyl, furyl, indolyl, benzothienyl, benzofuryl, imidazolyl, pyrazolyl, 2-thiazolyl, quinolinyl and 4-(2-benzyloxazolyl); or a pharmaceutically acceptable salt thereof.

39. (Twice amended) A method for treating inflammation or an inflammation-mediated disorder, wherein said inflammation or inflammation-mediated disorder is mediated by a cyclooxygenase-2, comprising administering to a subject in need of such treatment an effective amount of a compound according to [claim 13] formula I:



wherein:

X is a group of formula II:



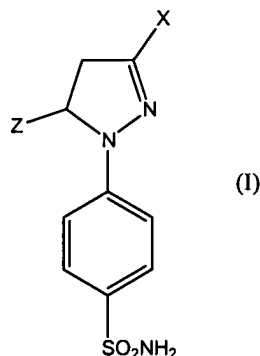
wherein:

R₃ and R₄ are independently selected from the group consisting of hydrogen, C₁-C₆ alkyl and C₁-C₆ alkoxy;

Z is selected from the group consisting of phenyl; phenyl monosubstituted with halogen, hydroxyl, nitro or carboxy; disubstituted phenyl; trisubstituted phenyl; and

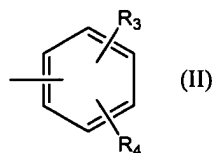
heteroaryl selected from the group consisting of substituted and unsubstituted pyridyl, furyl, indolyl, benzothienyl, benzofuryl, imidazolyl, pyrazolyl, 2-thiazolyl, quinoliny and 4-(2-benzyloxazolyl); or a pharmaceutically acceptable salt thereof.

40. (Twice amended) A method for treating a neoplasia, wherein said neoplasia is mediated by a cyclooxygenase-2, comprising administering to a subject in need of such treatment an effective amount of a compound of the formula I



wherein:

X is selected from the group consisting of trihalomethyl, C₁-C₆ alkyl, and a group of formula II:



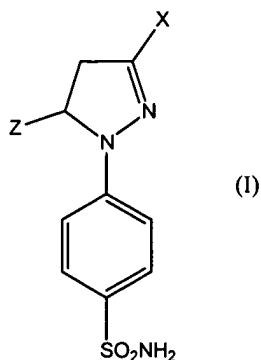
wherein:

R₃ and R₄ are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C₁-C₆ alkyl; C₁-C₆ alkoxy; carboxy; C₁-C₆ trihaloalkyl; and cyano;

Z is selected from the group consisting of substituted and unsubstituted [aryl] heteroaryl; phenyl, mono- or di-substituted with hydroxyl, nitro, or carboxy; and tri-substituted phenyl;

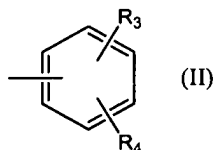
or a pharmaceutically acceptable salt thereof.

41. (Amended) A method for treating an angiogenesis-mediated disorder, wherein said angiogenesis-mediated disorder is mediated by a cyclooxygenase-2, administering to a subject in need of such treatment an effective amount of a compound of the formula:



wherein:

X is selected from the group consisting of trihalomethyl, C₁-C₆ alkyl, and a group of formula II:



wherein:

R₃ and R₄ are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C₁-C₆ alkyl; C₁-C₆ alkoxy; carboxy; C₁-C₆ trihaloalkyl; and cyano;

Z is selected from the group consisting of substituted and unsubstituted aryl; or a pharmaceutically acceptable salt thereof.

42. (Original) A method according to claim 40 or 41 wherein Z is selected from the group consisting of substituted and unsubstituted heteroaryl; or a pharmaceutically acceptable salt thereof.

43. (Amended) A method according to claim 42 wherein [[Z]] said heteroaryl is selected from the group consisting of substituted and unsubstituted indolyl, furyl, thienyl, pyridyl, benzofuryl, benzothienyl, imidazolyl, pyrazolyl, thiazolyl, benzothiazolyl, quinolinyl, and 4-(2-benzyloxazolyl); or a pharmaceutically acceptable salt thereof.

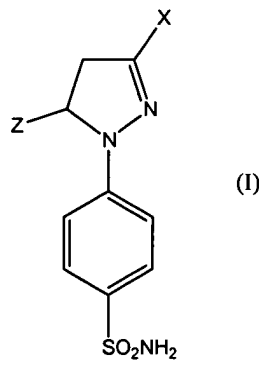
44. (Original) A method according to claim 43 wherein Z is substituted or unsubstituted 3-indolyl; or a pharmaceutically acceptable salt thereof.

45. (Original) A method according to claim 40 or 41 wherein X is trifluoromethyl.

46. (Original) A method according to claim 40 or 41 wherein X is a group according to formula II wherein R₃ and R₄ are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C₁-C₆ alkyl; C₁-C₆ alkoxy; carboxy; C₁-C₆ trihaloalkyl; and cyano; or a pharmaceutically acceptable salt thereof.

47. (Original) A method according to claim 46 wherein Z is selected from the group consisting of unsubstituted phenyl; and mono-, di- and tri-substituted phenyl.

48. (New) A compound of the formula I:



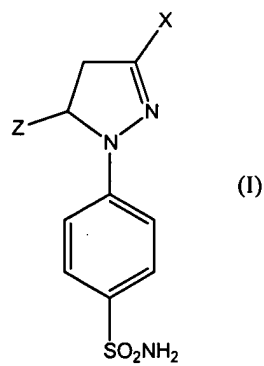
wherein:

X is C₁-C₆ alkyl; and

Z is selected from the group consisting of substituted and unsubstituted aryl other than substituted and unsubstituted phenyl;

provided when Z is heteroaryl, it is selected from the group consisting of substituted and unsubstituted pyridyl, indolyl, benzothienyl, benzofuryl, imidazolyl, pyrazolyl, 2-thiazolyl, quinoliny and 4-(2-benzyloxazolyl); or a pharmaceutically acceptable salt thereof.

49. (New) A method for producing a compound of formula I:



wherein:

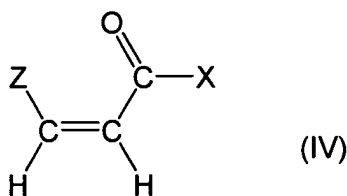
the group X is C₁-C₆ alkyl; and

Z is selected from the group consisting of substituted and unsubstituted aryl, other than substituted and unsubstituted phenyl;

provided when Z is heteroaryl, it is selected from the group consisting of substituted and unsubstituted pyridyl, indolyl, benzothienyl, benzofuryl, imidazolyl, pyrazolyl, 2-thiazolyl, quinoliny and 4-(2-benzyloxazolyl);

the method comprising:

(a) reacting a compound of the formula IV:

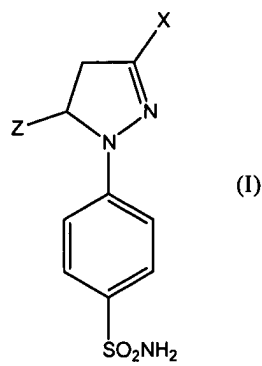


wherein X and Z are so defined;

with 4-sulfamyl phenyl hydrazine or a salt thereof; and

(b) isolating a compound according to formula I from the reaction products.

50. (New) An isolated optical isomer of a compound of the formula I:

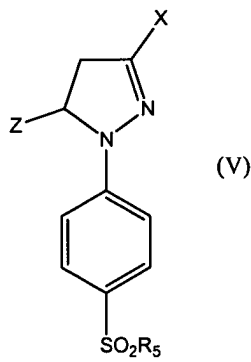


wherein:

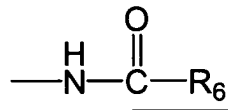
X is selected from the group consisting of trihalomethyl and C₁-C₆ alkyl;

Z is selected from the group consisting of substituted and unsubstituted heteroaryl; phenyl that is mono-substituted or di-substituted with substituents independently selected from the group consisting of hydroxyl, nitro, and carboxy; and phenyl that is tri-substituted; or a pharmaceutically acceptable salt thereof.

51. (New) A method for producing a compound of formula V:

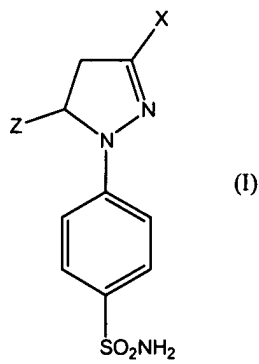


wherein R₅ is:

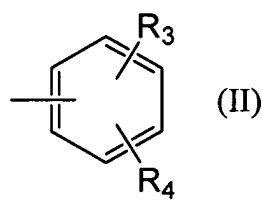


wherein R₆ is C₁-C₆ alkyl; or a pharmaceutically acceptable salt thereof; the method comprising:

(a) reacting a compound of formula I:



wherein X is selected from the group consisting of trihalomethyl, C₁-C₆ alkyl and a group of the formula II:

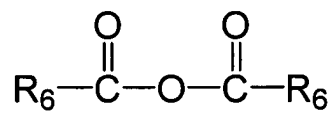


wherein:

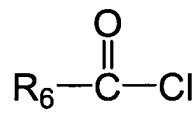
R₃ and R₄ are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C₁-C₆ alkyl; C₁-C₆ alkoxy; carboxy; C₁-C₆ trihaloalkyl; and cyano; and

Z is substituted or unsubstituted heteroaryl;

with an anhydride of the formula:



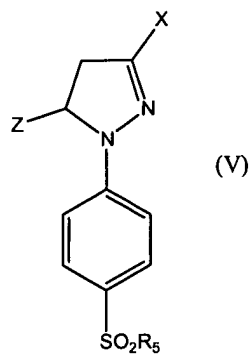
or an acylating compound of the formula:



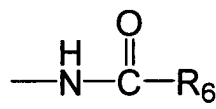
wherein R₆ is C₁-C₆ alkyl; and

(b) isolating a compound according to formula V from the reaction products.

52. (New) A method for producing a compound of formula V:

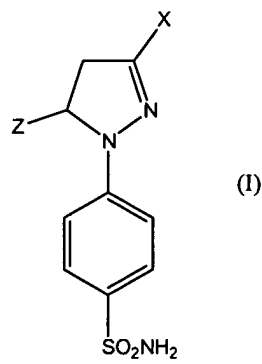


wherein R₅ is:

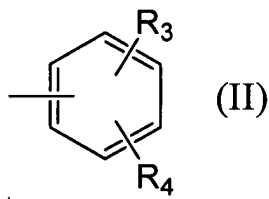


wherein R₆ is C₁-C₆ alkyl; or a pharmaceutically acceptable salt thereof; the method comprising:

(a) reacting a compound of formula I:



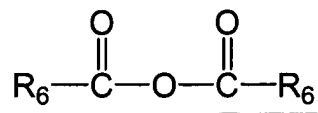
wherein X is a group of the formula II:



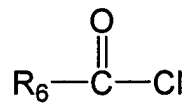
wherein: R₃ and R₄ are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C₁-C₆ alkyl; C₁-C₆ alkoxy; carboxy; C₁-C₆ trihaloalkyl; and cyano; and

Z is substituted or unsubstituted aryl;

with an anhydride of the formula:



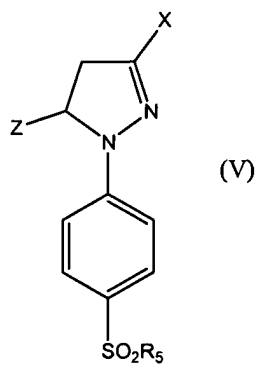
or an acylating compound of the formula:



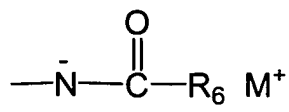
wherein R_6 is $\text{C}_1\text{-C}_6$ alkyl; and

(b) isolating a compound according to formula V from the reaction products.

53. (New) A method for producing a compound of formula V:

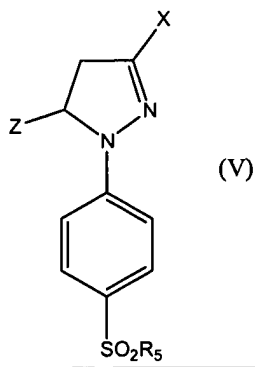


wherein R_5 is:

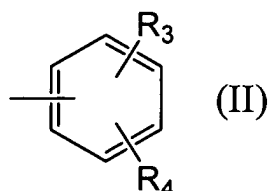


wherein R_6 is $\text{C}_1\text{-C}_6$ alkyl and M is Na, K or Li; or a pharmaceutically acceptable salt thereof; the method comprising:

(a) reacting a compound of formula I:

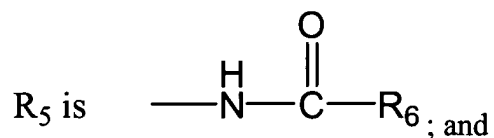


wherein X is selected from the group consisting of trihalomethyl, C₁-C₆ alkyl and a group of the formula II:



wherein: R₃ and R₄ are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C₁-C₆ alkyl; C₁-C₆ alkoxy; carboxy; C₁-C₆ trihaloalkyl; and cyano; and

Z is substituted or unsubstituted heteroaryl; and

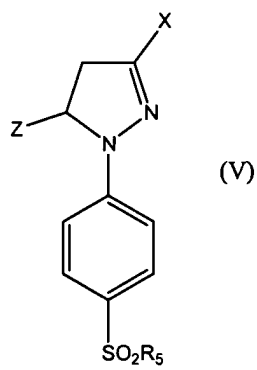


wherein R₆ is as defined above,

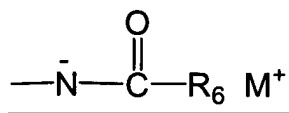
with an alkali hydroxide selected from the group consisting of NaOH, KOH and LiOH; and

(b) isolating a compound according to formula V from the reaction products.

54. (New) A method for producing a compound of formula V:

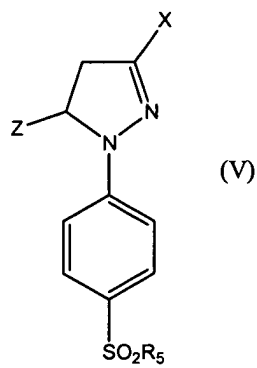


wherein R₅ is:

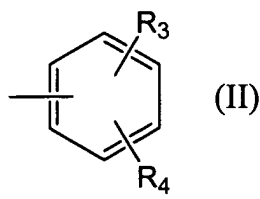


wherein R₆ is C₁-C₆ alkyl and M is Na, K or Li; or a pharmaceutically acceptable salt thereof; the method comprising:

(a) reacting a compound of formula I:

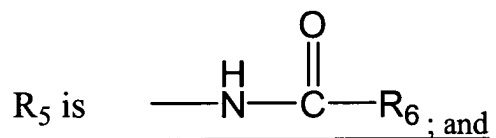


wherein X is a group of the formula II:



wherein: R₃ and R₄ are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C₁-C₆ alkyl; C₁-C₆ alkoxy; carboxy; C₁-C₆ trihaloalkyl; and cyano; and

Z is substituted or unsubstituted aryl; and



wherein R₆ is as defined above,

with an alkali hydroxide selected from the group consisting of NaOH, KOH and LiOH;
and

(b) isolating a compound according to formula V from the reaction products.